Ligation of the perforating vein for treatment of steal syndrome in arteriovenous grafts: a hypothesis

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To the Editor: Regarding the article by Goel *et al.*,[1] we want to mention a few points.

In the valuable paper by Goel *et al.*,[1] a new technique called minimally invasive limited ligation endoluminal-assisted revision (MILLER) was introduced as the first-line treatment for the management of steal syndrome. Their technique not only eliminates difficulties of previous approaches for the management of steal phenomenon, but also reduces the rate of closing arteriovenous fistula (AVF) due to decline in the blood flow of vascular access. In a study by Morsey *et al.*,[2] the incidence of steal syndrome was even higher for arteriovenous grafts (AVGs; 4.3 vs 1.8% for AVFs), and this poses more difficulties for vascular surgeons in countries where AVGs are used more frequently.

We have shown that the creation of side-to-side elbow AVFs diverts blood flow of the artery to the deep veins through the perforating vein due to lower resistance of the deep veins.[3] To solve this problem, we introduced a simple but efficient technique involving ligation of the perforating vein. This method can be used as both a therapeutic and a preventive strategy and was associated with salvage of 80% of AVFs in a small series.[4] With respect to the lower resistance of the deep veins, it seems that a similar phenomenon occurs after inserting AVGs as well. Thus, ligation of the perforating vein may be effective for treatment and prevention of steal syndrome in AVGs. Moreover, as shown in Figure 1, the perforating vein can be approached by a small incision and this procedure is 'minimal invasive'. This is just a hypothesis and has to be tested.

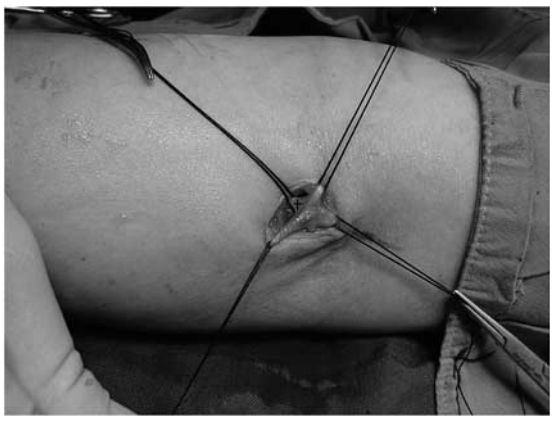

Figure 1 | The perforating vein is approached by an incision about 1.5–2 cm below the antecubital crease. The perforating vein is the vein without string.

1. Goel N, Miller GA, Jotwani MC *et al.* Minimally invasive limited ligation endoluminal-assisted revision (MILLER) for treatment of dialysis access-associated steal syndrome. *Kidney Int* 2006; **70**: 765–770.
2. Morsy AH, Kulbaski M, Chen C *et al.* Incidence and characteristics of patients with hand ischemia after a hemodialysis access procedure. *J Surg Res* 1998; **74**: 8–10.
3. Moini M, Williams GM, Pourabbasi MS *et al.* Side-to-side arterio-venous fistula at the elbow with perforating vein ligation. *J Vasc Surg* 2008; **47**: 1274–1278.
4. Moini M, Rasouli MR, Nouri M. Ligation of the perforating vein: a treatment for steal syndrome in side-to-side elbow arteriovenous fistula. *Ann Vasc Surg* 2008; **22**: 307.

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Response to 'Ligation of the perforating vein for treatment of steal syndrome in arteriovenous grafts: a hypothesis'

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Moini *et al.*[1] have developed a procedure that increases access resistance by simply eliminating flow decompression into the deep veins. The authors assert that an access with dialysis-associated steal syndrome can be corrected by eliminating decompression into the deep venous system. This is an accurate assertion given the resistance in the access circuit will be higher and therefore shunt less blood. However, the degree to which the resistance in the shunt is altered cannot be incrementally controlled. This type of imprecision caused the failures of traditional banding, DRIL and RUDI procedures. If deep-vein ligation increases the intra-access pressure too much, the access will thrombose. Furthermore, even if the procedure provides relief from steal symptoms, this may only be temporary because the superficial veins may hypertrophy over time. This hypertrophy may result in increased shunt as the access matures. Steal symptoms may return and will require further intervention (MILLER procedure) to restore resistance balance.

If the superficial outflow system becomes thrombosed or problematic, as it frequently does, prior ligation of the perforating vein limits alternate outflow possibilities. This is one of the reasons a graft has a shorter life span than a fistula. A fistula has a surgical beginning and frequently two, three, or four outflow veins. A graft has limited outflow possibilities as compared with a fistula, making it much more susceptible to stenosis and thrombosis. Any A-V access venous drainage should include all possible outflows to maximize longevity. Limiting an outflow system by ligating the deep vein is likely to reduce the durability and reliability of the access. Possibly, increasing

thrombosis rates to decrease a syndrome, which affects only 1–8% of the accesses, seems to have an unfavorable risk benefit profile.

The MILLER measured, standardized banding procedure is successful because it allows for precise application of resistance into a system.[2] This procedure is minimally invasive and can be performed multiple times just as easily as it can be undone by simply dilating the band with an angioplasty balloon. Ligation of the perforating vein definitely seems to be a good idea in helping the superficial veins to mature. However, it is unlikely to achieve a high level of success in the treatment and prevention of DASS. Although it is a feasible treatment, limited precision of flow volume reduction and irreversibility lead to the same problems that made traditional banding procedures unsuccessful.

1. Moini M, Rasouli M. Ligation of the perforating vein for treatment of steal syndrome in arteriovenous grafts: a hypothesis. *Kidney Int* 2008; **74**: 826.
2. Goel N, Miller GA, Jotwani MC *et al.* Minimally invasive limited ligation endoluminal-assisted revision (MILLER) for treatment of dialysis access-associated steal syndrome. *Kidney Int* 2006; **70**: 765–770.

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The effect of epoetin dose on hematocrit

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To the Editor: Cotter *et al.*[1] used United States Renal Data System data from 14,001 incident patients to estimate the dose–response relationship between epoetin (EPO) and hematocrit. The authors used their analysis to infer the maximum effective EPO dose and suggested that this should inform Federal reimbursement policy. However, the analytic approach used is inconsistent with FDA guidance and the inferred maximum dose is not likely to be generalizable to the US dialysis population. We think it is inadvisable to support reimbursement policies based on inferential information without careful consideration of the potential clinical consequences.

When there is a time delay in clinical response (for example, hemoglobin) following dosing, FDA recommends parallel dose–response studies where patients receive constant doses over fixed time periods with no target ceiling, such as that proposed by Eschbach *et al.*[2] However, Cotter *et al.*[3] used observational data containing frequent EPO dose titrations, analyzed with marginal structural modeling. In studies of flexible dosing, FDA recommends employing mixed-effects regression, which accounts for interpatient variability in EPO responsiveness. This is important because a broad range of EPO doses (~40-fold) are required to achieve target hemoglobin levels in individuals.[4] The application of unconventional analytics using observational data should not supplant knowledge gained by the established approach of controlled clinical trials designed to estimate dose–response. Inferring a maximum effective dose from an estimated mean might result in inadequate dosing for many patients. Any new EPO policy should be based on the most rigorous data and analyses, with careful assessment of the potential impact.

1. Cotter D, Zhang Y, Thamer M *et al.* The effect of epoetin dose on hematocrit. *Kidney Int* 2008; **73**: 347–353.
2. Eschbach JW, Egrie JC, Downing MR *et al.* Correction of the anemia of end-stage renal disease with recombinant human erythropoietin. Results of a combined phase I and II clinical trial. *N Engl J Med* 1987; **316**: 73–78.
3. Guideline for industry. Dose–response information to support drug registration. http://www.fda.gov/cder/guidance/iche4.pdf Accessed December 17, 2007.
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Response to 'Regarding ''the effect of epoetin dose on hematocrit''.'

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Critchlow *et al.*[1] state that 'the application of unconventional analytics using observational data should not supplant knowledge gained via the established approach of controlled clinical trials designed to estimate dose–response.' We agree. However, controlled trials might not provide a generalizable dose–response curve if more sick patients who require higher doses of erythropoiesis stimulating agents are under-represented because of restricted enrollment criteria, patient's underlying disease burden, etc. Therefore, controlled trials based on such restrictions are likely to underestimate the range of erythropoiesis stimulating agent dose required in the general hemodialysis population.

In contrast, our analysis of dose–response uses data from an unselected medicare population and over the dose range currently used by clinicians. We would encourage Amgen and others to attempt to resolve the dose–response issue with appropriately designed clinical trials in a heterogeneous population. In the absence of such trials,